

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: B.C. Askew, et al.

Serial No.: To be Assigned (Case No. 20009YDB)

Art Unit:

1611

Filed: July 27, 2001

Examiner:

For: INTEGRIN RECEPTOR ANTAGONISTS

To be assigned

Assistant Commissioner for Patents

Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

The above identified case is a divisional application related to pending U.S.S.N. 09/453,847, filed December 2, 1999.

Please enter this Preliminary Amendment into the above-captioned application and consider the following remarks.

IN THE SPECIFICATION:

On page 1, in the Cross-Reference to Related Applications, delete the text "This application is a divisional of Serial No. 09/212,082, filed December 15, 1998, which in turn is related to US provisional applications Serial No. 60/069,899, filed December 17, 1997; 60/083,209, filed April 27, 1998; 60/092,622, filed July 13, 1998; and 60/108,063, filed November 12, 1998; the contents of all of which are hereby incorporated by reference." and insert therefor the following text:

~~DATE OF DEPOSIT~~
DATE OF DEPOSIT July 27, 2001
~~EXPRESS MAIL NO.~~
EXPRESS MAIL NO. EL 503909058115
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS
BEING DEPOSITED WITH THE UNITED STATES POSTAL
SERVICE AS EXPRESS MAIL, "POST OFFICE TO
ADDRESSEE" BEFORE 5 P.M. ON THE ABOVE DATE IN
AN ENVELOPE ADDRESSED TO ASSISTANT COMMISSIONER
FOR PATENTS, WASHINGTON, D.C. 20231.
MAILED BY SPB Crowley
DATE 7-27-01

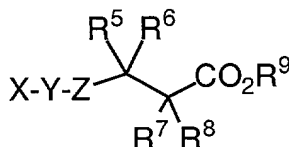
-- This application is a divisional of Serial No. 09/454,847, filed December 2, 1999, which is a divisional of Serial No. 09/212,082, filed December 15, 1998, which in turn is related to US provisional applications Serial No. 60/069,899, filed December 17, 1997; 60/083,209, filed April 27, 1998; 60/092,622, filed July 13, 1998; and 60/108,063, filed November 12, 1998; the contents of all of which are hereby incorporated by reference. --

IN THE CLAIMS:

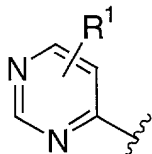
CANCEL Claims 1-40

ADD Claims 41-63

41. A compound of the formula

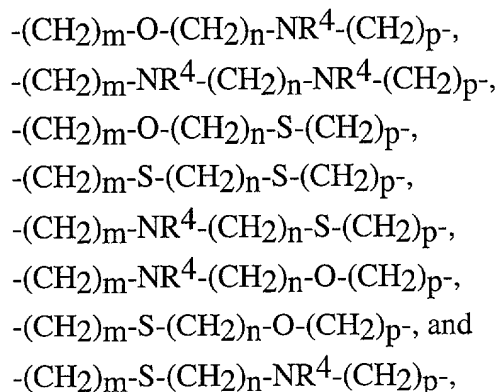


wherein X is



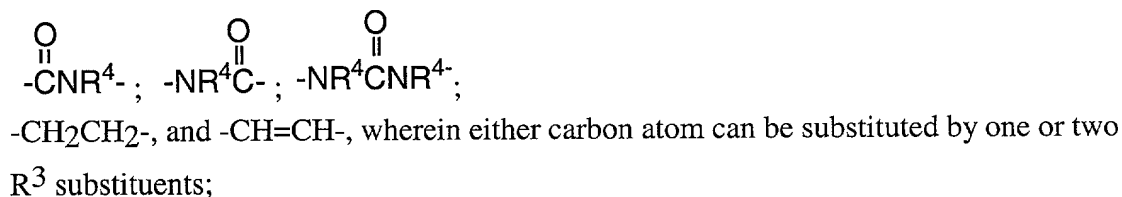
Y is selected from the group consisting of

- (CH₂)_m-,
- (CH₂)_m-O-(CH₂)_n-,
- (CH₂)_m-NR⁴-(CH₂)_n-,
- (CH₂)_m-S-(CH₂)_n-,
- (CH₂)_m-SO-(CH₂)_n-,
- (CH₂)_m-SO₂-(CH₂)_n-,
- (CH₂)_m-O-(CH₂)_n-O-(CH₂)_p-,



wherein any methylene (CH_2) carbon atom in Y, other than in R^4 , can be substituted by one or two R^3 substituents, with the proviso that when Y is $-(\text{CH}_2)_m\text{-NR}^4\text{-(CH}_2)_n\text{-}$ and $n = 1$, then the R^3 substituent on the methylene carbon in $-(\text{CH}_2)_m\text{-}$ adjacent to the nitrogen cannot be oxo;

Z is selected from the group consisting of



R^1 and R^2 are each independently selected from the group consisting of

hydrogen, halogen, C_{1-10} alkyl, C_{3-8} cycloalkyl,
 C_{3-8} cycloheteroalkyl, C_{3-8} cycloalkyl C_{1-6} alkyl,
 C_{3-8} cycloheteroalkyl C_{1-6} alkyl, aryl, aryl C_{1-8} alkyl, amino,
amino C_{1-8} alkyl, C_{1-3} acylamino, C_{1-3} acylamino C_{1-8} alkyl,
 $(\text{C}_{1-6}$ alkyl) $_p$ amino, $(\text{C}_{1-6}$ alkyl) $_p$ amino C_{1-8} alkyl,
 C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-6} alkyl, hydroxycarbonyl,
hydroxycarbonyl C_{1-6} alkyl, C_{1-3} alkoxycarbonyl,
 C_{1-3} alkoxycarbonyl C_{1-6} alkyl, hydroxycarbonyl-
 C_{1-6} alkyloxy, hydroxy, hydroxy C_{1-6} alkyl, C_{1-6} alkyloxy-
 C_{1-6} alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy,

trifluoroethoxy, C₁₋₈ alkyl-S(O)_p, (C₁₋₈alkyl)_paminocarbonyl,
C₁₋₈ alkyloxycarbonylamino, (C₁₋₈ alkyl)_paminocarbonyloxy,
(aryl C₁₋₈ alkyl)_pamino, (aryl)_pamino, aryl C₁₋₈
alkylsulfonylamino, and C₁₋₈ alkylsulfonylamino;

or two R¹ substituents, when on the same carbon atom, are taken together with the carbon
atom to which they are attached to form a carbonyl group;

each R³ is independently selected from the group consisting of

hydrogen,
aryl,
C₁₋₁₀ alkyl,
aryl-(CH₂)_r-O-(CH₂)_s-,
aryl-(CH₂)_rS(O)_p-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-(CH₂)_s-,
halogen,
hydroxyl,
oxo,
trifluoromethyl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₅ alkoxy,
C₁₋₅ alkoxy carbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,
C₁₋₆ alkylcarbonyloxy,
C₃₋₈ cycloalkyl,
(C₁₋₆ alkyl)_pamino,
amino C₁₋₆ alkyl,
arylaminocarbonyl,
aryl C₁₋₅ alkylaminocarbonyl,
aminocarbonyl,

aminocarbonyl C₁₋₆ alkyl,
hydroxycarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
HC≡C-(CH₂)_t-,
C₁₋₆ alkyl-C≡C-(CH₂)_t-,
C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
aryl-C≡C-(CH₂)_t-,
C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
CH₂=CH-(CH₂)_t-,
C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
aryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkyl-SO₂-(CH₂)_t-,
C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
C₁₋₆ alkoxy,
aryl C₁₋₆ alkoxy,
aryl C₁₋₆ alkyl,
(C₁₋₆ alkyl)_pamino C₁₋₆ alkyl,
(aryl)_pamino,
(aryl)_pamino C₁₋₆ alkyl,
(aryl C₁₋₆ alkyl)_pamino,
(aryl C₁₋₆ alkyl)_pamino C₁₋₆ alkyl,
arylcarbonyloxy,
aryl C₁₋₆ alkylcarbonyloxy,
(C₁₋₆ alkyl)_paminocarbonyloxy,
C₁₋₈ alkylsulfonylamino,
arylsulfonylamino,
C₁₋₈ alkylsulfonylamino C₁₋₆ alkyl,
arylsulfonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonylamino,
aryl C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl,

C₁₋₈ alkoxycarbonylamino,
C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
aryloxy carbonylamino C₁₋₈ alkyl,
aryl C₁₋₈ alkoxycarbonylamino,
aryl C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
C₁₋₈ alkylcarbonylamino,
C₁₋₈ alkylcarbonylamino C₁₋₆ alkyl,
arylcarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonylamino,
aryl C₁₋₆ alkylcarbonylamino C₁₋₆ alkyl,
aminocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)_paminocarbonylamino,
(C₁₋₈ alkyl)_paminocarbonylamino C₁₋₆ alkyl,
(aryl)_paminocarbonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)_paminocarbonylamino,
(aryl C₁₋₈ alkyl)_paminocarbonylamino C₁₋₆ alkyl,
aminosulfonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)_paminosulfonylamino,
(C₁₋₈ alkyl)_paminosulfonylamino C₁₋₆ alkyl,
(aryl)_paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)_paminosulfonylamino,
(aryl C₁₋₈ alkyl)_paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylsulfonyl,
C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
arylsulfonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcarbonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,

(aryl C₁₋₈ alkyl)_paminocarbonyl C₁₋₆ alkyl;

carbon atom or atoms to which R³ is attached is itself attached to no more than one heteroatom;

each R^4 is independently selected from the group consisting of

aryl C₁₋₈ alkoxycarbonyl,

C₁₋₈ alkylcarbonyl,
arylcabonyl,
aryl C₁₋₆ alkylcarbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,
aminosulfonyl,
C₁₋₈ alkylaminosulfonyl,
(aryl)_paminosulfonyl,
(aryl C₁₋₈ alkyl)_paminosulfonyl,
arylsulfonyl,
arylC₁₋₆ alkylsulfonyl,
C₁₋₆ alkylthiocarbonyl,
arylthiocarbonyl, and
aryl C₁₋₆ alkylthiocarbonyl,

wherein any of the alkyl groups of R⁴ are either unsubstituted or substituted with one to three R¹ substituents;

R⁵ and R⁶ are each independently selected from the group consisting of

hydrogen,
C₁₋₁₀ alkyl,
aryl,
aryl-(CH₂)_r-O-(CH₂)_s-,
aryl-(CH₂)_rS(O)_p-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-(CH₂)_s-,
halogen,
hydroxyl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₅ alkoxy,
C₁₋₅ alkoxycarbonyl,
(C₁₋₈ alkyl)_paminocarbonyl,

C₁₋₆ alkylcarbonyloxy,
C₃₋₈ cycloalkyl,
(C₁₋₆ alkyl)_pamino,
amino C₁₋₆ alkyl,
arylaminocarbonyl,
aryl C₁₋₅ alkylaminocarbonyl,
aminocarbonyl,
aminocarbonyl C₁₋₆ alkyl,
hydroxycarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
HC≡C-(CH₂)_t-,
C₁₋₆ alkyl-C≡C-(CH₂)_t-,
C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
aryl-C≡C-(CH₂)_t-,
C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
CH₂=CH-(CH₂)_t-,
C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
aryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkyl-SO₂-(CH₂)_t-,
C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
C₁₋₆ alkoxy,
aryl C₁₋₆ alkoxy,
aryl C₁₋₆ alkyl,
(C₁₋₆ alkyl)_pamino C₁₋₆ alkyl,
(aryl)_pamino,
(aryl)_pamino C₁₋₆ alkyl,
(aryl C₁₋₆ alkyl)_pamino,
(aryl C₁₋₆ alkyl)_pamino C₁₋₆ alkyl,
arylcarbonyloxy,
aryl C₁₋₆ alkylcarbonyloxy,

(C1-6 alkyl)paminocarbonyloxy,
C1-8 alkylsulfonylamino,
arylsulfonylamino,
C1-8 alkylsulfonylamino C1-6 alkyl,
arylsulfonylamino C1-6 alkyl,
aryl C1-6 alkylsulfonylamino,
aryl C1-6 alkylsulfonylamino C1-6 alkyl,
C1-8 alkoxycarbonylamino,
C1-8 alkoxycarbonylamino C1-8 alkyl,
aryloxycarbonylamino C1-8 alkyl,
aryl C1-8 alkoxycarbonylamino,
aryl C1-8 alkoxycarbonylamino C1-8 alkyl,
C1-8 alkylcarbonylamino,
C1-8 alkylcarbonylamino C1-6 alkyl,
arylcabonylamino C1-6 alkyl,
aryl C1-6 alkylcarbonylamino,
aryl C1-6 alkylcarbonylamino C1-6 alkyl,
aminocarbonylamino C1-6 alkyl,
(C1-8 alkyl)paminocarbonylamino,
(C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
(aryl)paminocarbonylamino C1-6 alkyl,
(aryl C1-8 alkyl)paminocarbonylamino,
(aryl C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
aminosulfonylamino C1-6 alkyl,
(C1-8 alkyl)paminosulfonylamino,
(C1-8 alkyl)paminosulfonylamino C1-6 alkyl,
(aryl)paminosulfonylamino C1-6 alkyl,
(aryl C1-8 alkyl)paminosulfonylamino,
(aryl C1-8 alkyl)paminosulfonylamino C1-6 alkyl,
C1-6 alkylsulfonyl,
C1-6 alkylsulfonyl C1-6 alkyl,
arylsulfonyl C1-6 alkyl,

aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcarbonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl,
(aryl)paminocarbonyl C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminocarbonyl, and
(aryl C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl;

or R⁵ and R⁶ are taken together with the carbon atom to which they are attached to form a carbonyl group,

wherein any of the alkyl groups of R⁵ or R⁶ are either unsubstituted or substituted with one to three R¹ substituents, and provided that each R⁵ and R⁶ are selected such that in the resultant compound the carbon atom to which R⁵ and R⁶ are attached is itself attached to no more than one heteroatom;

R⁷ and R⁸ are each independently selected from the group consisting of

hydrogen,
C₁₋₁₀ alkyl,
aryl,
aryl-(CH₂)_r-O-(CH₂)_s-,
aryl-(CH₂)_rS(O)_p-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-(CH₂)_s-,
aryl-(CH₂)_r-C(O)-N(R⁴)-(CH₂)_s-,
aryl-(CH₂)_r-N(R⁴)-C(O)-(CH₂)_s-,

aryl-(CH₂)_t-N(R⁴)-(CH₂)_s-,
halogen,
hydroxyl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₅ alkoxy,
C₁₋₅ alkoxycarbonyl,
(C₁₋₈ alkyl)paminocarbonyl,
C₁₋₆ alkylcarbonyloxy,
C₃₋₈ cycloalkyl,
(C₁₋₆ alkyl)pamino,
amino C₁₋₆ alkyl,
arylamino carbonyl,
aryl C₁₋₅ alkylamino carbonyl,
aminocarbonyl,
aminocarbonyl C₁₋₆ alkyl,
hydroxycarbonyl,
hydroxycarbonyl C₁₋₆ alkyl,
HC≡C-(CH₂)_t-,
C₁₋₆ alkyl-C≡C-(CH₂)_t-,
C₃₋₇ cycloalkyl-C≡C-(CH₂)_t-,
aryl-C≡C-(CH₂)_t-,
C₁₋₆ alkylaryl-C≡C-(CH₂)_t-,
CH₂=CH-(CH₂)_t-,
C₁₋₆ alkyl-CH=CH-(CH₂)_t-,
C₃₋₇ cycloalkyl-CH=CH-(CH₂)_t-,
aryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkylaryl-CH=CH-(CH₂)_t-,
C₁₋₆ alkyl-SO₂-(CH₂)_t-,
C₁₋₆ alkylaryl-SO₂-(CH₂)_t-,
C₁₋₆ alkoxy,
aryl C₁₋₆ alkoxy,
aryl C₁₋₆ alkyl,

(C1-6 alkyl)pamino C1-6 alkyl,
(aryl)pamino,
(aryl)pamino C1-6 alkyl,
(aryl C1-6 alkyl)pamino,
(aryl C1-6 alkyl)pamino C1-6 alkyl,
arylcarbonyloxy,
aryl C1-6 alkylcarbonyloxy,
(C1-6 alkyl)paminocarbonyloxy,
C1-8 alkylsulfonylamino,
arylcarbonylamino,
arylsulfonylamino,
C1-8 alkylsulfonylamino C1-6 alkyl,
arylsulfonylamino C1-6 alkyl,
aryl C1-6 alkylsulfonylamino,
aryl C1-6 alkylsulfonylamino C1-6 alkyl,
C1-8 alkoxycarbonylamino,
C1-8 alkoxycarbonylamino C1-8 alkyl,
aryloxycarbonylamino C1-8 alkyl,
aryl C1-8 alkoxycarbonylamino,
aryl C1-8 alkoxycarbonylamino C1-8 alkyl,
C1-8 alkylcarbonylamino C1-6 alkyl,
arylcarbonylamino C1-6 alkyl,
aryl C1-6 alkylcarbonylamino,
aryl C1-6 alkylcarbonylamino C1-6 alkyl,
aminocarbonylamino C1-6 alkyl,
arylaminocarbonylamino,
(C1-8 alkyl)paminocarbonylamino,
(C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
(aryl)paminocarbonylamino C1-6 alkyl,
(aryl C1-8 alkyl)paminocarbonylamino,
(aryl C1-8 alkyl)paminocarbonylamino C1-6 alkyl,
aminosulfonylamino C1-6 alkyl,

(C₁₋₈ alkyl)paminosulfonylamino,
(C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
(aryl)paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminosulfonylamino,
(aryl C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylsulfonyl,
C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
arylsulfonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonyl,
aryl C₁₋₆ alkylsulfonyl C₁₋₆ alkyl,
C₁₋₆ alkylcarbonyl,
C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
arylcarbonyl C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonyl,
aryl C₁₋₆ alkylcarbonyl C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl,
(aryl)paminocarbonyl C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminocarbonyl,
(aryl C₁₋₈ alkyl)paminocarbonyl C₁₋₆ alkyl, and
C₇₋₂₀ polycyclyl C₀₋₈ alkylsulfonylamino,

wherein any of the alkyl groups of R⁷ and R⁸ are either unsubstituted or substituted with one to three R¹ substituents, and provided that each R⁷ and R⁸ are selected such that in the resultant compound the carbon atom to which R⁷ and R⁸ are attached is itself attached to no more than one heteroatom;

R⁹ is selected from the group consisting of
hydrogen,

C₁₋₈ alkyl,
aryl,
aryl C₁₋₈ alkyl,
C₁₋₈ alkylcarbonyloxy C₁₋₄ alkyl,
aryl C₁₋₈ alkylcarbonyloxy C₁₋₄ alkyl,
C₁₋₈ alkylaminocarbonylmethylene, and
C₁₋₈ dialkylaminocarbonylmethylene;

wherein

each m is independently an integer from 0 to 6;
each n is independently an integer from 0 to 6;
each p is independently an integer from 0 to 2;
each r is independently an integer from 1 to 3;
each s is independently an integer from 0 to 3; and
each t is independently an integer from 0 to 3;

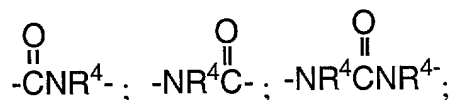
and the pharmaceutically acceptable salts thereof.

42. The compound of Claim 41 wherein Y is selected from the group consisting of

$-(CH_2)_m-$,
 $-(CH_2)_m-O-(CH_2)_n-$,
 $-(CH_2)_m-NR^4-(CH_2)_n-$,
 $-(CH_2)_m-S-(CH_2)_n-$,
 $-(CH_2)_m-SO-(CH_2)_n-$,
 $-(CH_2)_m-SO_2-(CH_2)_n-$,
 $-(CH_2)_m-O-(CH_2)_n-O-(CH_2)_p-$,
 $-(CH_2)_m-O-(CH_2)_n-NR^4-(CH_2)_p-$,
 $-(CH_2)_m-NR^4-(CH_2)_n-NR^4-(CH_2)_p-$, and
 $-(CH_2)_m-NR^4-(CH_2)_n-O-(CH_2)_p-$,

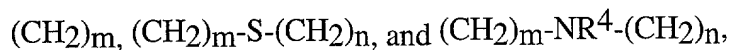
wherein any methylene (CH₂) carbon atom in Y, other than in R⁴, can be substituted by one or two R³ substituents, with the proviso that when Y is -(CH₂)_m-NR⁴-(CH₂)_n- and n = 1, then the R³ substituent on the methylene carbon in -(CH₂)_m- adjacent to the nitrogen cannot be oxo;

and Z is selected from the group consisting of



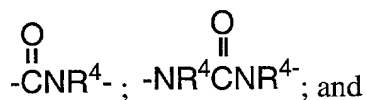
-CH₂CH₂-, and -CH=CH-, wherein either carbon atom can be substituted by one or two R³ substituents.

43. The compound of Claim 44 wherein Y is selected from the group consisting of



wherein any methylene (CH₂) carbon atom in Y, other than in R⁴, can be substituted by one or two R³ substituents, with the proviso that when Y is -(CH₂)_m-NR⁴-(CH₂)_n- and n = 1, then the R³ substituent on the methylene carbon in -(CH₂)_m- adjacent to the nitrogen cannot be oxo;

and Z is selected from the group consisting of



-CH₂CH₂-, wherein either carbon atom can be substituted by one or two R³ substituents.

44. The compound of Claim 43 wherein each R³ is independently selected from the group consisting of

hydrogen,
fluoro,

trifluoromethyl,
aryl,
C₁₋₈ alkyl,
arylC₁₋₆ alkyl
hydroxyl,
oxo,
arylaminocarbonyl,
aryl C₁₋₅ alkylaminocarbonyl,
aminocarbonyl, and
aminocarbonyl C₁₋₆ alkyl;

and each R⁴ is independently selected from the group consisting of

hydrogen,
aryl,
C₃₋₈ cycloalkyl,
C₁₋₈ alkyl,
C₁₋₈ alkylcarbonyl,
arylcarbonyl,
C₁₋₆ alkylsulfonyl,
arylsulfonyl,
arylC₁₋₆alkylsulfonyl,
arylC₁₋₆alkylcarbonyl,
C₁₋₈alkylaminocarbonyl,
arylC₁₋₅alkylaminocarbonyl,
arylC₁₋₈alkoxycarbonyl, and
C₁₋₈alkoxycarbonyl.

45. The compound of Claim 44 wherein R⁶, R⁷, and R⁸ are each hydrogen and R⁵ is selected from the group consisting of
hydrogen,
aryl,
C₁₋₈ alkyl,

aryl-C \equiv C-(CH₂)_t-,
aryl C₁₋₆ alkyl,
CH₂=CH-(CH₂)_t-, and
HC \equiv C-(CH₂)_t-.

46. The compound of Claim 45 wherein R⁹ is selected from the group consisting of hydrogen, methyl, and ethyl.

47. The compound of Claim 46 wherein R⁹ is hydrogen.

48. The compound of Claim 44 wherein R⁵, R⁶, and R⁸ are each hydrogen and R⁷ is selected from the group consisting of

hydrogen,
aryl,
C₁₋₈ alkylcarbonylamino,
C₁₋₈ alkylsulfonylamino,
arylcarbonylamino,
arylsulfonylamino,
C₁₋₈ alkylsulfonylamino C₁₋₆ alkyl,
arylsulfonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylsulfonylamino,
aryl C₁₋₆ alkylsulfonylamino C₁₋₆ alkyl,
C₁₋₈ alkoxycarbonylamino,
C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
aryloxycarbonylamino C₁₋₈ alkyl,
aryl C₁₋₈ alkoxycarbonylamino,
aryl C₁₋₈ alkoxycarbonylamino C₁₋₈ alkyl,
C₁₋₈ alkylcarbonylamino C₁₋₆ alkyl,
arylcarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylcarbonylamino,
aryl C₁₋₆ alkylcarbonylamino C₁₋₆ alkyl,
aminocarbonylamino C₁₋₆ alkyl,

(C₁₋₈ alkyl)paminocarbonylamino,
(C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
(aryl)paminocarbonylamino C₁₋₆ alkyl,
arylamino carbonylamino,
(aryl C₁₋₈ alkyl)paminocarbonylamino,
(aryl C₁₋₈ alkyl)paminocarbonylamino C₁₋₆ alkyl,
aminosulfonylamino C₁₋₆ alkyl,
(C₁₋₈ alkyl)paminosulfonylamino,
(C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
(aryl)paminosulfonylamino C₁₋₆ alkyl,
(aryl C₁₋₈ alkyl)paminosulfonylamino,
(aryl C₁₋₈ alkyl)paminosulfonylamino C₁₋₆ alkyl,
C₁₋₆ alkylthiocarbonylamino,
C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl,
arylthiocarbonylamino C₁₋₆ alkyl,
aryl C₁₋₆ alkylthiocarbonylamino,
aryl C₁₋₆ alkylthiocarbonylamino C₁₋₆ alkyl, and
C₇₋₂₀ polycyclyl C₀₋₈ alkylsulfonylamino.

49. The compound of Claim 48 wherein R⁵, R⁶, and R⁸ are each hydrogen and R⁷ is selected from the group consisting of

hydrogen,
aryl,
C₁₋₈ alkylcarbonylamino,
aryl C₁₋₆ alkylcarbonylamino,
arylcarbonylamino,
C₁₋₈ alkylsulfonylamino,
aryl C₁₋₆ alkylsulfonylamino,
arylsulfonylamino,
C₁₋₈ alkoxy carbonylamino,
aryl C₁₋₈ alkoxy carbonylamino,
arylamino carbonylamino,

(C₁₋₈ alkyl)_paminocarbonylamino,
(aryl C₁₋₈ alkyl)_paminocarbonylamino,
(C₁₋₈ alkyl)_paminosulfonylamino, and
(aryl C₁₋₈ alkyl)_paminosulfonylamino.

50. The compound according to Claim 49 wherein R⁹ is selected from the group consisting of hydrogen, methyl, and ethyl.

51. The compound according to Claim 50 wherein R⁹ is hydrogen.

52. The compound of Claim 44 which is:

3-[5-(2-Amino-pyrimidin-4-yl)-pentanoylamino]-3(S)-(quinolin-3-yl)-propionic acid;

and the pharmaceutically acceptable salts thereof.

53. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 41 and a pharmaceutically acceptable carrier.

54. The composition of Claim 53 which further comprises an active ingredient selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) a cytotoxic/antiproliferative agent,
- d) a matrix metalloproteinase inhibitor,
- e) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- f) an inhibitor of VEGF,
- g) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1,
- h) a cathepsin K inhibitor, and
- i) a farnesyl transferase inhibitor or a geranylgeranyl transferase inhibitor or a dual farnesyl/geranylgeranyl transferase inhibitor;

and mixtures thereof.

55. The composition of Claim 54 wherein said active ingredient is selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator, and
- c) a cathepsin K inhibitor;
and mixtures thereof.

56. The composition of Claim 55 wherein said organic bisphosphonate or pharmaceutically acceptable salt or ester thereof is alendronate monosodium trihydrate.

57. The composition of Claim 54 wherein said active ingredient is selected from the group consisting of

- a) a cytotoxic/antiproliferative agent,
- b) a matrix metalloproteinase inhibitor,
- c) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- d) an inhibitor of VEGF,
- e) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1, and
- f) a cathepsin K inhibitor;
and mixtures thereof.

58. A method of eliciting an integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 41.

59. The method of Claim 58 wherein the integrin receptor antagonizing effect is an $\alpha v\beta 3$ antagonizing effect.

60. The method of Claim 59 wherein the $\alpha v \beta 3$ antagonizing effect is selected from the group consisting of inhibition of bone resorption, restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammation, viral disease, tumor growth, and metastasis.

61. The method of Claim 60 wherein the $\alpha v \beta 3$ antagonizing effect is the inhibition of bone resorption.

62. A method of inhibiting bone resorption in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 53.

63. A method of inhibiting bone resorption in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 55.

REMARKS

Subsequent to the Restriction Requirement for U.S.S.N. 09/453,847 made final November 13, 2000 (Paper No. 4), the Applicants elected for examination the subject matter of Group I, holding in abeyance the non-elected subject matter of Groups II, III, and IV for further prosecution in a divisional application. The Applicants are now filing such a divisional application directed to the non-elected subject matter of Group IV.

Claims 1-40 of the parent application have been cancelled and replaced with new claims 41-63 directed to the non-elected subject matter of Group IV. The newly added Claims 41-63 do not contain new matter and are fully supported by Applicants' specification.

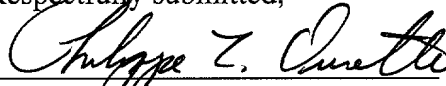
The section "CROSS REFERENCE TO RELATED APPLICATIONS" has been amended to indicate the priority of the present application.

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The Examiner is respectfully requested to enter the above amendment and begin prosecution on the merits.

Respectfully submitted,

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Enclosure

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